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Retinal phospholipase C from squid is a regulator of Gqa GTPase activity

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Abstract

The phospholipase C (PLC) pathway is the major signaling mechanism of photoactivation in invertebrate photoreceptors.

Here we report the cloning of a cDNA encoding a 140-kDa retinal PLC that is uniquely expressed in squid photoreceptors. This cDNA encodes a protein with multiple distinct modular domains: PH, X and Y catalytic, and C2 domains, as well as G- and P-box motifs and two GTP/ATP binding motifs.

The PLC was stimulated by activated squid Gqa but not by squid Gqbg or mammalian β g subunits. The PLC was inhibited by monophosphate, diphosphate and triphosphate nucleotides but not cyclic nucleosides. We also tested the

ability of PLC-140 to regulate the GTPase activity of Gqa in the rhabdomeric membranes. Depletion of PLC-140 from the rhabdomeric membranes decreased the GTP hydrolysis but not GTP γ S binding to the membranes. Reconstitution of purified PLC-140 with membranes accelerated Gqa GTPase activity by 5-fold at a concentration of 2.5 μ M. These results suggest that PLC-140 plays an important role in both the activation and inactivation pathways of invertebrate visual transduction.

Keywords: Gqa, GTPase, phospholipase C, photoreceptor, squid.

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The phosphoinositide-specific phospholipase C (PLC) enzymes are a family of proteins that hydrolyze membrane phosphoinositide-4,5-bisphosphate, to generate the second messengers inositol-1,4,5-trisphosphate (IP₃) and diacylglycerol (DAG). PLC proteins are found in both vertebrate and invertebrate species as well as in yeast, slime molds,

species including: *Musca* (DeVary et al. 1987), *Limulus* (Fein 1986), and squid (Mitchell et al. 1995; Suzuki et al. 1995). Several invertebrate PLCs have been cloned and include two PLC isoforms from *Drosophila melanogaster*: PLC-norpA and PLC-p21 (Bloomquist et al. 1988; Shortridge et al. 1991), and one from lobster (Xu and

fungi and plants (Rebecchi and Pentylä 2000). Thus far, 11 mammalian PLCs have been identified and they have been classified into four distinct groups: PLC-β, PLC-γ, PLC-δ and PLC-1. Of these four classes, the PLC-β and PLC-1 isozymes demonstrate G protein-regulated activity. The PLC-β type enzymes are regulated by G protein α subunits of the Gq family (Kozasa et al. 1993; Lee and Rhee 1995; Biddlecome et al. 1996), as well as by G protein βγ subunits (Waldo et al. 1991; Park et al. 1993a; Wu et al. 1993b) while PLC-1 is regulated by monomeric Ras (Kelley et al. 2001).

The PLC pathway is the major signaling pathway in invertebrate photoreceptors. The molecular mechanism entails the photoactivation of rhodopsin leading to the stimulation of invertebrate Gq, which in turn activates retinal PLC. The role of G protein-regulated PLC activity in vision has been studied most extensively in photoreceptors of *Drosophila* (Bloomquist et al. 1988; Running Deer et al. 1995), but have also been reported in other invertebrate

(McClintock 1999). A cDNA encoding a truncated PLC enzyme was also isolated from squid (Carne et al. 1999). We have previously reported the isolation and purification of a 140-kDa PLC protein from squid photoreceptors and shown it to be regulated by Gqα (Mitchell et al. 1995). We report the cloning of the full-length cDNA encoding a 140-kDa PLC protein and demonstrate its regulation by protein subunits and nucleotides as well as its ability to regulate the GTPase activity of invertebrate Gqα.

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Abbreviations used: DAG, diacylglycerol; IP3, inositol-1,4,5-trisphosphate; PLC, phospholipase C.

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Squid phospholipase C is a Gqα GAP 1

Materials and methods

Cloning of squid phospholipase C

Oligonucleotide primers were designed based on previously published peptide sequences derived from a purified 140-kDa PLC protein (Mitchell et al. 1995). PCR reactions were performed using a squid retinal cDNA library as template (a generous gift from Drs J. K. Northup and M. Brownstein of NIH, Bethesda, MD, USA). A 472 base pair PCR product was generated that showed high sequence similarity to a truncated squid PLC (Carne et al. 1995) and primers based on the sequence from this truncated PLC produced a fragment of approximately 2600 base pairs. Further sequence information on the 3' end of the PLC cDNA was obtained using primers based on peptide four from purified PLC-140, and RACE (Sambrook and Russell 2001) reactions were performed to obtain the 5' and 3' UTRs using the gene-specific primers GCCTTAAATCAACAAAGCTTATACCAAAATTAT; TCC-AGTACAAGAAATATCCCTTGGGATCAA and the vector-specific primers TAATACGACTCACTATAGGGAGACCGGAAG; AAGGTTCTTCACAAAGATCTCTAGATC. Nucleotide sequences were determined for both strands of several positive clones

nitrocellulose membranes and immunoblotted with a polyclonal antibody raised against purified endogenous squid PLC-140 (Towbin et al. 1979).

Rhabdomic membrane and purified protein preparations

Photoreceptor membranes were prepared from frozen eyes taken from freshly caught *Loligo pealei* obtained from the Marine Biology Institute (Woods Hole, MA, USA) as previously described (Mitchell et al. 1995). The concentration of Gqα in the membranes was determined by quantitative immunoblotting using an antibody raised against the C-terminal sequence of Gqα (Upstate Biotechnology, Lake Placid, NY, USA) using recombinant squid Gqα as standard as previously described (Mitchell and Bansal 1997). PLC-140, Gqα and Gbg were purified from squid eyes as previously described (Mitchell et al. 1995; Bamsey et al. 2000).

Mammalian Gb₁₂ was purified from bovine ROS as described (Fung et al. 1992). Purified proteins were assessed by Coomassie blue staining following SDS-PAGE and determined to be >90% homogeneous.

GTPγS binding, GTPase and phospholipase C assays

GTPγS binding to rhabdomic membrane preparations was

from each PCR reaction by automated DNA sequencing at a local facility. The full-length sequence obtained (GenBank accession number AF258528) was compared with DNA sequences in GenBank. Simple Modular Architecture Research Tool (SMART) was used to determine the domain topology of the protein encoded by the cDNA (Schultz et al. 2000) and PROSITE database search (Hofmann et al. 1999) was used to identify biologically significant sites encoded by the cDNA. PESTfind program (Rogers et al. 1986; Rechsteiner and Rogers 1996) was used to identify PEST sequences in PLC-140.

Expression of recombinant PLC-140 in *Escherichia coli*

The protein encoded by the PLC-140 cDNA was expressed in BL21-SI cells using Gibco BRL Gateway Cloning Technology (Gibco-BRL, Gaithersburg, MD, USA). The full-length coding region of PLC-140 cDNA was PCR amplified using Clontech Advantage HF-2 PCR kit (Clontech Laboratories, Palo Alto, CA, USA) with attB1-FS and attB2-FA primers. Entry clones were generated in DH5α cells using the full-length attB PCR product and attP containing pDONR201 vector. Plasmid DNA from positive entry clones were isolated and used to generate His-tagged expression clones in pDEST17 vectors.

Bacterial BL21-SI colonies expressing His-tagged PLC-140 were induced with 0.3 M NaCl. PLC-140 protein expression was analyzed via western blotting using antiserum raised against purified PLC-140. Recombinant PLC-140 (rPLC-140) protein was purified from bacterial extracts under denaturing conditions (8.0 M urea, 10 mM Tris pH 8.0, 100 mM NaH₂PO₄, 500 mM NaCl) with Ni-NTA resin (Qiagen, Valencia, CA, USA) with slight modifications to manufacturer's instructions. The resin was washed in buffer containing 6 M urea, 20 mM Tris pH 8.0, 500 mM NaCl, 50 mM imidazole, and the proteins renatured using a stepwise gradient from 6 to 0 M urea in 20 mM Tris pH 8.0, 500 mM NaCl in 0.5 M increments prior to elution. The semipurified recombinant PLC protein (PLC was assessed as approximately 50% of the protein content of eluted fractions) was analyzed by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) on 8% polyacrylamide gels (Laemmli 1970), transferred to

determined by incubating 5 mg of membranes in 20 mM NaHEPES pH 7.5, 3 mM MgCl₂, 200 nM GTPγS (50 000 cpm/pmol) at 20°C for 10 min. At times indicated in individual experiments, binding reactions were stopped by dilution with 2 mL of ice-cold stop buffer (20 mM NaHEPES pH 7.5, 3 mM MgCl₂, 100 mM NaCl, 10 mM EDTA, 10 mM EGTA, 10 mM DTT, 10 mM β-mercaptoethanol, 10 mM PIP₂, 10 mM PIP₃, 10 mM PIP₄, 10 mM PIP₅, 10 mM PIP₆, 10 mM PIP₇, 10 mM PIP₈, 10 mM PIP₉, 10 mM PIP₁₀, 10 mM PIP₁₁, 10 mM PIP₁₂, 10 mM PIP₁₃, 10 mM PIP₁₄, 10 mM PIP₁₅, 10 mM PIP₁₆, 10 mM PIP₁₇, 10 mM PIP₁₈, 10 mM PIP₁₉, 10 mM PIP₂₀, 10 mM PIP₂₁, 10 mM PIP₂₂, 10 mM PIP₂₃, 10 mM PIP₂₄, 10 mM PIP₂₅, 10 mM PIP₂₆, 10 mM PIP₂₇, 10 mM PIP₂₈, 10 mM PIP₂₉, 10 mM PIP₃₀, 10 mM PIP₃₁, 10 mM PIP₃₂, 10 mM PIP₃₃, 10 mM PIP₃₄, 10 mM PIP₃₅, 10 mM PIP₃₆, 10 mM PIP₃₇, 10 mM PIP₃₈, 10 mM PIP₃₉, 10 mM PIP₄₀, 10 mM PIP₄₁, 10 mM PIP₄₂, 10 mM PIP₄₃, 10 mM PIP₄₄, 10 mM PIP₄₅, 10 mM PIP₄₆, 10 mM PIP₄₇, 10 mM PIP₄₈, 10 mM PIP₄₉, 10 mM PIP₅₀, 10 mM PIP₅₁, 10 mM PIP₅₂, 10 mM PIP₅₃, 10 mM PIP₅₄, 10 mM PIP₅₅, 10 mM PIP₅₆, 10 mM PIP₅₇, 10 mM PIP₅₈, 10 mM PIP₅₉, 10 mM PIP₆₀, 10 mM 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Fig. 2 Expression of PLC-140 in native and recombinant systems.

Samples of rhabdomeric membranes (Rhabs) or of washed rhabdomeric membranes (W-Rhabs) containing 1.6 pmoles Gq, 0.08 mg of purified endogenous PLC-140 (nPLC-140), 1 mL of an extract from *E. coli* transformed with a cDNA encoding his-tagged PLC-140 (bExt) and 30 mL of the extract following purification over Ni-affinity column (rPLC-140), were subjected to western blot analysis with an antibody raised against purified PLC-140. Dashes on the right side of the figure indicate the migration of molecular weight standards from top: a₂-macroglobulin (180 000), b-galactosidase (116 000), fructose-6-phosphate kinase (84 000), pyruvate kinase (58 000), fumarase (48 500), lactic dehydrogenase (36 500) and triosephosphate isomerase (26 600).

expressed in retinal photoreceptors; mammalian PLC-b4 and *Drosophila* norpA. The four peptides derived from purified PLC-140 on which the oligonucleotide primers were based were all present within the cDNA. When transformed into *E. coli* the cDNA encoding PLC-140 produced a protein that was similar in size to the native PLC found in squid membranes as well as the PLC purified from these membranes. The recombinant protein was

Fig. 3 Tissue distribution of PLC-140. Homogenates prepared from various squid tissues (10 mg for retina and 30 mg for all other tissues) were subjected to SDS PAGE followed by western blot analysis with an antibody raised against purified PLC-140. Dashes on the right side of the figure indicate the migration of molecular weight standards from top: a₂-macroglobulin (180 000), b-galactosidase (116 000), fructose-6-phosphate kinase (84 000), pyruvate kinase (58 000), fumarase (48 500), and lactic dehydrogenase (36 500).

similarity was found as anticipated to the truncated northern European squid PLC (Carne et al. 1995). PLC-140 also had significant similarity with the two *Drosophila* PLCs: norpA and PLC-21 (37%), and a recently identified PLC from lobster (35%) (Xu and McClintock 1999). Identity of PLC-140 with the mammalian PLC isozymes of the b family ranged between 39 and 40% with PLC-b1 and b4, and 36±39% identity with PLC-b2 and b3.

The domain structure of PLC-140 as determined using SMART module was found to include six distinct domains: pleckstrin homology (PH), X and Y catalytic, C2, G- and P-boxes. There were also two ATP/GTP-binding site motifs

recognized by an antibody raised against purified PLC-140 as demonstrated by western blot analysis (Fig. 2).

Comparison of the deduced amino acid sequence of this PLC with other sequences in the database revealed the protein to be similar in structure and organization to other members of the PLC- β family of proteins. Highest sequence

identified within the PLC sequence (Fig. 1b).

A survey of tissues taken from *Loligo pealei* by immunoblot using a polyclonal antibody raised against purified PLC-140 demonstrated expression of this protein only in the eye (Fig. 3). Neither the peripheral tissues nor the optic ganglion demonstrated any immune reactivity to

Fig. 1 (a) Alignment of the deduced amino acid sequence of squid PLC-140 (AF258528) with *Drosophila* norpA PLC (norpA: AF181641) and rat PLC- β 4 (A48047). The asterisks denote conserved amino acid residues in all the aligned sequences, the dots denote residues that are conserved in two or more proteins and the double dots denote conservative amino acid substitutions. The dashes represent gaps introduced for optimal alignment. (b) Domain structure of

PLC-140. It contains six distinct modular domains: pleckstrin homology domain (PH: 22–144), PLC catalytic domains (X: 323–471 and Y: 514–630) and calcium binding domain (C2: 651–750). P- and G-box motifs span amino acids 1016–1047 and 1069–1096, respectively. A putative PEST sequence region (score 1.3.26) designates the putative site of calpain cleavage (858–881) and * designates ATP/GTP binding site motifs (344–351 and 815–822).

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Table 1 [³⁵ S]GTPγS binding to purified PLC-140

Additions	[³⁵ S]GTPγS
None	100 ± 9
GMP 1 mM	18 ± 3
GDP 1 mM	34 ± 12
GTP 1 mM	25 ± 4
GTPγS 1 mM	19 ± 5
cGMP 1 mM	137 ± 13
ATP 1 mM	43 ± 12
cAMP 1 mM	128 ± 15
Mg ²⁺ 10 mM	99 ± 4
Ca ²⁺ 1 mM	123 ± 14

A total of 2 ng of purified PLC-140 were incubated with 120,000 cpm [³⁵ S]GTPγS (923,000 cpm/pmol) for 30 min in the presence of the indicated compounds. Samples were quenched and [³⁵ S]GTPγS bound to PLC-140 determined as described in Materials and methods. Results are shown as percentage of [³⁵ S] bound to PLC-140 in the absence of additional compounds (4.3 ± 0.4 fmol GTPγS bound) and are the mean ± SD of triplicate determinations.

activity approximately 70% over basal activity. Addition of the same concentration of Gqa activated by AIF resulted

Fig. 4 Regulation of PLC-140 activity by G proteins and ribonucleo-

tides. (a) Purified endogenous PLC-140 (2 ng) was incubated with phospholipid vesicles containing PIP₂ in the absence (control) or presence of 1 ng of Gqα, 1 mM NaF, 2 mM AlCl₃ (AIF control), 1 ng of activated Gq (Gqα-AIF), 10 ng of Gbg purified from squid rhabdomic membranes, or 175 ng of Gbg purified from bovine ROS. (b) Purified PLC-140 was assessed in the absence (control) or presence of the indicated compounds at a final concentration of 0.1 or 1 mM as described under Materials and methods. The results are means ± SD of two experiments and are expressed as a percentage of the activity in the absence of G protein subunits or nucleotides. The activity in control samples corresponding to 100% was 15 ± 2 pmol/min and 17 ± 3 pmol/min in experiments a and b, respectively.

the PLC antibody, indicating that the expression of this PLC protein is very specific to the squid photoreceptors.

Regulation of PLC-140 by Gqα, Gbg and nucleotides

The similarity in structure between PLC-140 and the other retinal PLC-β isozymes, norpA and PLC-β4, suggested that squid retinal PLC may show a similar pattern of regulation as these other proteins. We tested the effect of both squid and mammalian visual Gbg on endogenous purified PLC-140 in reconstitution assays and compared this to the activation seen by Gqα subunits that we have reported previously. Addition of 0.45 nM Gqα stimulated the PLC

increased activation of PLC-140 to 10-fold stimulation the basal activity of PLC-140 in the presence of AIF alone (Fig. 4a). Addition of a molar excess of either squid 6 nM Gbg or 100 nM mammalian retinal Gbg inhibited the PLC activity. The presence of GTP/ATP binding motif in the PLC-140 sequence suggested that nucleotides may regulate its activity and this was demonstrated for both guanine and adenine nucleotides that were both found to inhibit PLC activity in a concentration-dependent manner (Fig. 4b). PLC-140 was able to bind with a stoichiometry of approximately 0.3 mole of GTPγS/mole PLC and this binding was inhibited by unlabeled guanine monophosphate, guanine diphosphate and guanine triphosphate as well as adenosine triphosphate; however, cyclic adenosine monophosphate or cyclic guanine monophosphate were not able to displace GTPγS. Binding of nucleotide PLC-140 was unaffected by the presence of magnesium was slightly enhanced in the presence of calcium (Table

PLC regulation of Gqα GTPase activity

PLC-β1 has previously been demonstrated to increase the rate of GTP hydrolysis of mammalian Gqα (Chidiac and Ross 1999). Given the similarity between the squid Gqα protein and its mammalian counterparts of the Gq family (Ryba et al. 1993) we decided to test the effect of PLC on the GTPase activity of squid Gqα. The squid Gqα protein binds GTP very rapidly in the presence of light activated rhodopsin but extremely slowly when removed from the rhabdomic membranes, with rate constants for GTPγS

Fig. 5 [³⁵ S]GTPγS binding and GTPase activity of rhabdomeric and washed rhabdomeric membranes. (a) [³⁵ S]GTPγS binding to rhabdomeric membranes (B) or washed-rhabdomeric membranes (O) containing 1.6 pmoles Gqα was assessed for 0±60 s as described under Materials and methods. Reactions were stopped and [³⁵ S]GTPγS bound to membranes was counted and plotted as a function of time. (b) the Gqα GTPase activity of rhabdomeric and washed-rhabdomeric membranes was determined by incubating membranes with [³² P]GTP for 0±60 s as described under Materials and methods. Reactions were quenched and the ³² P_i-containing supernatants counted and plotted as a function of time. All values are the averages of duplicate reactions from representative experiments.

binding of 7.7/min and 0.23/min, respectively (data not shown). PLC-140 and other loosely associated proteins could be removed from the squid rhabdomeric membranes by washing in buffers containing 0.5 M NaCl (Fig. 2, W-Rhabs). We found no change in the GTPγS binding to the membranes following this washing procedure (Fig. 5a); however, there was a significant decrease in the rate of GTP hydrolysis in the washed membranes compared with the original rhabdomeric membranes (Fig. 5b). Reconstitution of purified endogenous PLC-140 with the washed membranes increased the GTPase activity 8-fold (Fig. 6a). When the stimulation of Gq GTPase activity was measured over a range of PLC-140 concentrations in the assay it was found that a molar ratio of PLC-140 : Gq of 2 : 1 was required in order to have any effect on GTPase activity.

Fig. 6 Regulation of Gqα GTPase activity by PLC-140. (a) The Gqα GTPase activity in washed-rhabdomeric membranes containing 2.5 pmoles Gqα was measured in the absence (B) or presence (O) of 20 pmoles of purified endogenous PLC-140 for 0±60 s as described under Materials and methods. ³² P_i was counted and plotted as the percentage of the maximal GTP hydrolysis as a function of time. (b) The effect of PLC-140 on Gqα GTPase activity was measured in washed-rhabdomeric membranes. Increasing concentrations of purified PLC-140 were added to the membranes containing 2.5 pmoles Gqα and the GTPase reaction was initiated at time 0 by the addition of [³² P]GTP. Reactions were stopped after 10 s by the addition of perchloric acid and ³² P_i counted and plotted as the percentage of maximal GTP hydrolysis. Data points are the means of duplicate samples and are representative of two separate experiments.

This GAP activity increased to a maximal effect seen with a 10±20-fold molar excess of PLC (Fig. 6b).

Discussion

A cDNA that encodes the PLC enzyme we have previously isolated from squid rhabdomeric membranes was isolated in this study. This PLC protein was only found in the squid eye and not identified in any other tissue from squid under the conditions that we have used in our study. PLC isozymes expressed in visual systems of other invertebrates have not been shown to have such specific tissue distribution. Lobster PLC-β was found to be widely expressed in many tissues (Xu and McClintock 1999) and *Drosophila* norpA, while predominantly expressed in the eye is also found in the optic

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Fig. 7 The role of PLC-140 regulation in visual transduction in squid photoreceptors. The model presents the molecular components of the squid visual system. Rhodopsin activation by light regulates GDP-GTP exchange on Gqα facilitating the Gqα activation of PLC-140. PLC activation increases the production of inositol 1,4,5-trisphosphate (IP3) and diacylglycerol (DAG) from inositol bisphosphate. IP3 stimulates the release of calcium from subrhabdomeric stores and the combination of calcium and DAG may lead to the opening of ion channels and depolarization of the membrane. Two reactions that limit the activation of this system are shown. First, the PLC-140 interaction with Gqα-GTP increases the rate of GTP hydrolysis by the Gqα protein, limiting the time of PLC activation by the Gqα protein. Second, the increase in calcium concentration stimulates a phosphodiesterase (PDE) in the squid photoreceptor leading to an increase in nucleotide concentrations that are inhibitory to PLC140 activity.

lobe and brain (Bloomquist et al. 1988). Further identification of the mRNA encoding the PLC enzyme and its expression in the various squid tissues is required to determine if the expression of the gene encoding PLC-140 is in fact eye-specific; however, the eye is clearly the site of highest expression of this protein.

The domain structure of PLC-140 was very similar to other PLC enzymes of the β family. As expected, the similarity between PLC-140 and other PLC-β enzymes is

and PLC-β2, and since we have shown that purified PLC-140 is activated by calcium and squid Gq, they may be sites for this regulation.

PLC-140 has a long carboxyl terminal region that contains the P-box and G-box motifs required for activation by G proteins (Lee et al. 1993; Park et al. 1993b; Wu et al. 1993a; Kim et al. 1996). The truncated squid PLC that was identified by Carne et al. (1995) lacked a carboxyl-terminal tail and does not encode P- or G-box motifs and may therefore not be sensitive to Gqα-dependent activation. In support of this notion, we have seen cleavage of purified PLC-140 by exogenous calpain with loss of Gqα regulatory (L. H. Mayeenuddin, unpublished data). Although we have not been able to obtain amino acid sequence from calpain digested PLC-140 fragments, cleavage of the protein in or near the putative PEST sequence which spans amino acids 858±881, positive PEST score of 3.26 (Sekhar and Free 1998), would produce protein fragments of approximate size observed by us and others (Suzuki et al. 1999). Carboxyl-terminal truncations have also been reported for mammalian PLC-β1, PLC-β3 and PLC-β4 (Park et al. 1993b; Banno et al. 1995; Kim et al. 1998). The effect of these truncations on PLC activation is enzyme-specific. Cleavage of PLC-β3 by calpain renders the truncated PLC more sensitive to regulation by G protein βγ subunits (Banno et al. 1995), while the C-terminally truncated sp variant of PLC-β4, PLC-β4b, has been shown to be insensitive to regulation by both Gqα and Gbg (Kim et al. 1998). The βγ sensitivity of the calpain-digested PLC-140 has not been tested; however, given the lack of βγ regulation of intact PLC-140 shown here, it seems unlikely that the truncated protein will be βγ-sensitive.

Two ATP/GTP binding sites were identified within the deduced amino acid sequence of PLC-140. The GHOLTGKS sequence found within the X domain of PLC-140 (amino acids 344±351) and the AAKPVKGK sequence (amino acids 814±822) located between the C domain and the P- and G-boxes, both correspond to the (G/A)X4GK(S/T) identified as one of the motifs found in members of the GTPase superfamily (Bourne et al. 1999). These are similar to the motifs found within PLC-β4 and norpA also within the X domains of these PLC isozymes (Lee et al. 1993). We have shown here that PLC-140 was able to bind guanine and adenine monophosphorylated,

greatest within the conserved X and Y catalytic domains (65±70% identity). These two regions are highly conserved amongst all PLC isozymes and they are essential for catalytic activity (Bristol et al. 1988; Ellis et al. 1993). The PH and C2 domains of PLC-140 represent structurally conserved protein modules, which in other PLC-β enzymes have been shown to be involved in diverse calcium and lipid interactions (Rizo and Sudhof 1998; Katan and Allen 1999). The PH and C2 domains of PLC-140 show 60±85% sequence similarity to the respective domains in PLC-β1

diphosphorylated and triphosphorylated nucleotides but cyclic nucleotides. Similar to PLC-β4 (Lee et al. 1994), guanine and adenine nucleotides inhibited the activity of PLC-140. It is possible that binding of nucleotides with the X domain could disrupt the catalytic activity of these enzymes.

The lack of PLC-140 regulation by G protein βγ subunits and inhibition by ribonucleotides, distinguishes this enzyme as a member of an emerging subgroup of PLC-β proteins involved in visual systems. It has been

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speculated that inhibition of PLC-β4 by monophosphate, diphosphate and triphosphate but not the cyclic nucleotides may be a mechanism for their regulation in the mammalian photoreceptors where the concentrations of GMP, GTP and cGMP are of course regulated by light (Lee et al. 1994). In the invertebrate visual systems, the major light-stimulated transduction pathway does not involve regulation of nucleotide hydrolysis, nevertheless, there have been reports of effects of guanine nucleotides in *Limulus* (Johnson et al. 1986) and squid (Saibil 1984) as well as a report of calcium-stimulated cGMP phosphodiesterase activity in squid eyes (Brown and Kelman 1996). Possibly, in the invertebrate eye, light regulates nucleotide concentrations via a PLC-stimulated rise in intracellular calcium and subsequent activation of cyclic nucleotide hydrolysis. Such a scheme is outlined in Fig. 7, where the nucleotide suppression of PLC activity is proposed as a mechanism to limit the activity of the PLC in the face of rising calcium levels and reduce the gain of the invertebrate visual system that occurs downstream of the PLC. If this mechanism exists then one would anticipate that inhibition of phosphodiesterase activity would lead to an increase in both the amplitude and duration of responses to light. Indeed, these were the findings when the PDE inhibitor zaprinast was introduced into *Limulus* photoreceptors (Johnson and O'Day 1995). These authors found that the effect of zaprinast was only seen in response to stimulation by bright light, required calcium and was upstream of IP₃ production. Clearly, there are alternative explanations for these observations and more

phospholipids and Gq protein α subunits, consistent with our observations of the regulation of purified PLC-140 protein. The demonstration that this protein can be inhibited by nucleotides and acts to limit the activity of its own stimulator, Gqα, suggests that PLC-140 plays a pivotal role in both the activation and inactivation of cephalopod visual systems.

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work is needed to test if regulation of PLC by nucleotides does exist in vivo in an invertebrate visual system.

We have also examined the effect of PLC-140 on Gqα activity by regulation of its GTPase activity. We first observed a change in GTPase activity of rhabdomeric membranes following removal of loosely associated proteins that include PLC-140. Reconstitution of purified PLC-140 back to these membranes in molar excess of Gqα increased the GTPase activity 10-fold. The requirement for an excess of PLC to Gqα in order to significantly influence the rate of inactivation of Gqα is in keeping with our estimates of a threefold molar excess of total PLC-140 to total Gqα in the whole squid eye. It is not difficult to envision that an even greater concentration of PLC could occur at specific sites within the microvillar structure in response to light stimulation. Recent studies in *Drosophila* have also shown dependence of GTPase activity of Gqα on the high concentrations of norp A PLC (Cook et al. 2000). It seems that feedback inhibition of invertebrate Gqα proteins by PLC is common to invertebrate visual systems and is required for single-photon responses in these systems.

In conclusion, we have cloned a cDNA encoding a PLC that appears to be the major effector of squid visual systems. This protein contains a number of identifiable domains that may be sites of interaction of PLC-140 with membranes,

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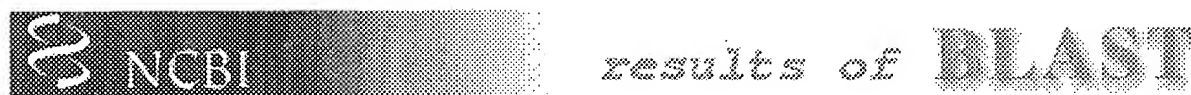
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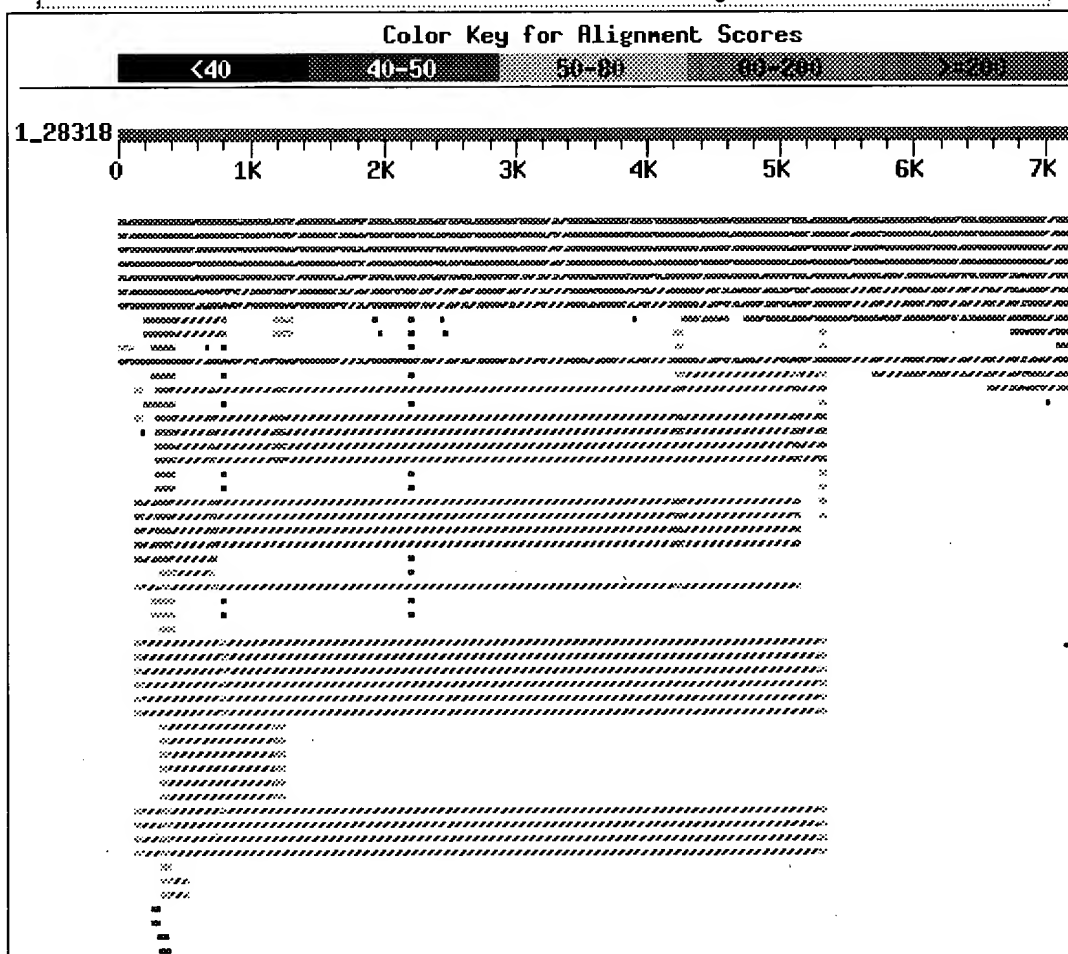
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cDNA

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Taxonomy reports**Distribution of 1012 Blast Hits on the Query Sequence**



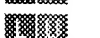











































Mouse-over to show define and scores. Click to show alignments



Score E

Sequences producing significant alignments:

(bits) Value

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gi 38084793 ref XM_129130.5 	Mus musculus spectrin beta 3 (...)	343	3e-90	
gi 5902121 ref NM_006946.1 	Homo sapiens spectrin, beta, no...	224	2e-54	
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gi 23271110 gb BC033305.1 	Mus musculus, clone IMAGE:401041...	224	2e-54	
gi 2511783 gb AF026489.1 AF026489	Mus musculus beta III spe...	224	2e-54	
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Alignments

Get selected sequences

Select all

Deselect all

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Query: 4173 ctggagagcctgcaggcccagctgcactcagatgactatggcaaggacctcaccagtgtc 4232

|||||
Sbjct: 4586 ctggagagcctgcaggcccagctgcactcagatgactatggcaaggacctcaccagtgtc 4645

Query: 4233 aacattctgctaaagaagcaacagatgctggaacgagagatggctgtgagatagaaggag 4292

|||||
Sbjct: 4646 aacattctgctaaagaagcaacagatgctggaacgagagatggctgtgagagagaaggag 4705

Query: 4293 gtagaggctatccaggcccaggcaaaagccctggcccaggaagaccaaagtgcaggagag 4352

|||||
Sbjct: 4706 gtagaggctatccaggcccaggcaaaagccctggcccaggaagaccaaagtgcaggagag 4765

Score = 285 bits (144), Expect = 6e-73
Identities = 144/144 (100%)
Strand = Plus / Plus

Query: 1903 cgtcgtctctggaggttcctctgggaagtgggtgaggccgaggcctgggttcgggagcag 1962

|||||
Sbjct: 2312 cgtcgtctctggaggttcctctgggaagtgggtgaggccgaggcctgggttcgggagcag 2371

Query: 1963 cagcacctcctggcctcagctgagacaggccgggacctgactgggtgtcctccgcctgctc 2022
|||||
Sbjct: 2372 cagcacctcctggcctcagctgagacaggccgggacctgactgggtgtcctccgcctgctc 2431

Query: 2023 aataagcacacagccctacgggggt 2046
|||||
Sbjct: 2432 aataagcacacagccctacgggggt 2455

Score = 278 bits (140), Expect = 1e-70
Identities = 143/144 (99%)
Strand = Plus / Plus

Query: 2719 gacatagctgagcagttgctgaaggccagtcaccaggcaaggaccgcatcattggcacc 2778
|||||
Sbjct: 3128 gacatagctgagcagttgctgaaggccagtcaccaggcaaggaccgcatcattggcacc 3187

Query: 2779 caggagcagctcaaccaaaggtggcagcagttcaggtccctggcaggtggcaaaaaggca 2838
|||||
Sbjct: 3188 caggagcagctcaaccaaaggtggcagcagttcaggtccctggcagatggcaaaaaggca 3247

Query: 2839 gctctgacatcagccctgagcatc 2862
|||||
Sbjct: 3248 gctctgacatcagccctgagcatc 3271

Score = 246 bits (124), Expect = 5e-61
Identities = 141/147 (95%), Gaps = 6/147 (4%)
Strand = Plus / Plus

Query: 5285 gagtgaaggacagtctcaatgaggcctgggctgacctgctggaggtggccctgctggac 5344
|||||
Sbjct: 5711 gagtgaaggacagtctcaatgaggcctgggctgacctgctggag-----ctgctggac 5764

Query: 5345 acaagaggtcaggtgctggctgctgcttatgagctgcagcgcttctgcatggggcccg 5404
|||||
Sbjct: 5765 acaagaggtcaggtgctggctgctgcttatgagctgcagcgcttctgcatggggcccg 5824

Query: 5405 caagccctggcacgggtgcagcacaag 5431
|||||
Sbjct: 5825 caagccctggcacgggtgcagcacaag 5851

Score = 240 bits (121), Expect = 3e-59
Identities = 121/121 (100%)
Strand = Plus / Plus

Query: 7091 gaaagagagcgagaaaaacgattcagcttctttaagaagaacaagtagttggggcaagac 7150
|||||
Sbjct: 7511 gaaagagagcgagaaaaacgattcagcttctttaagaagaacaagtagttggggcaagac 7570

Query: 7151 tcccaggccagctccctccctctgttcaggaaactgccagggactgtcgacagagaccac 7210
|||||
Sbjct: 7571 tcccaggccagctccctccctctgttcaggaaactgccagggactgtcgacagagaccac 7630

Query: 7211 c 7211
|
Sbjct: 7631 c 7631

Score = 222 bits (112), Expect = 7e-54
Identities = 135/144 (93%), Gaps = 9/144 (6%)
Strand = Plus / Plus

Query: 673 tttgagtcctgaagaagtgtaacgcacactacaatctgcagaatgctttcaatctggct 732
|||||
Sbjct: 1064 tttgagtcctgaagaagtgtaacgcacactacaatctgcagaatgctttcaatctggct 1123

Query: 733 gaaaaggaacttggcctgacgaagctcctggatcct-----aacgtagaccaaccc 783
|||||
Sbjct: 1124 gaaaaggaacttggcctgacgaagctcctggatcctgaagatgtgaacgtagaccaaccc 1183

Query: 784 gatgagaagtccatcatcacctac 807
|||||
Sbjct: 1184 gatgagaagtccatcatcacctac 1207

Score = 204 bits (103), Expect = 2e-48
Identities = 126/135 (93%), Gaps = 9/135 (6%)
Strand = Plus / Plus

Query: 6551 atgccccagagcagatcgtctgagtcagctcatgttgccaccctgccgcacgaggtgct 6610
|||||
Sbjct: 6971 atgccccagagcagatcgtctgagtcagctcatgttgccaccctgccgcacgaggtgct 7030

Query: 6611 gagctctctgctcaggaacagatggaaggg-----cgcaaacaggagatggaagcc 6661
|||||
Sbjct: 7031 gagctctctgctcaggaacagatggaagggacgctgtgccgcaaacaggagatggaagcc 7090

Query: 6662 ttcaataagaaagct 6676
|||||
Sbjct: 7091 ttcaataagaaagct 7105

Score = 180 bits (91), Expect = 2e-41
Identities = 91/91 (100%)

results of **BLAST**

BLASTX 2.2.6 [Apr-09-2003]

genomiz

RID: 1069188234-32305-140862554207.BLASTQ3

Query=

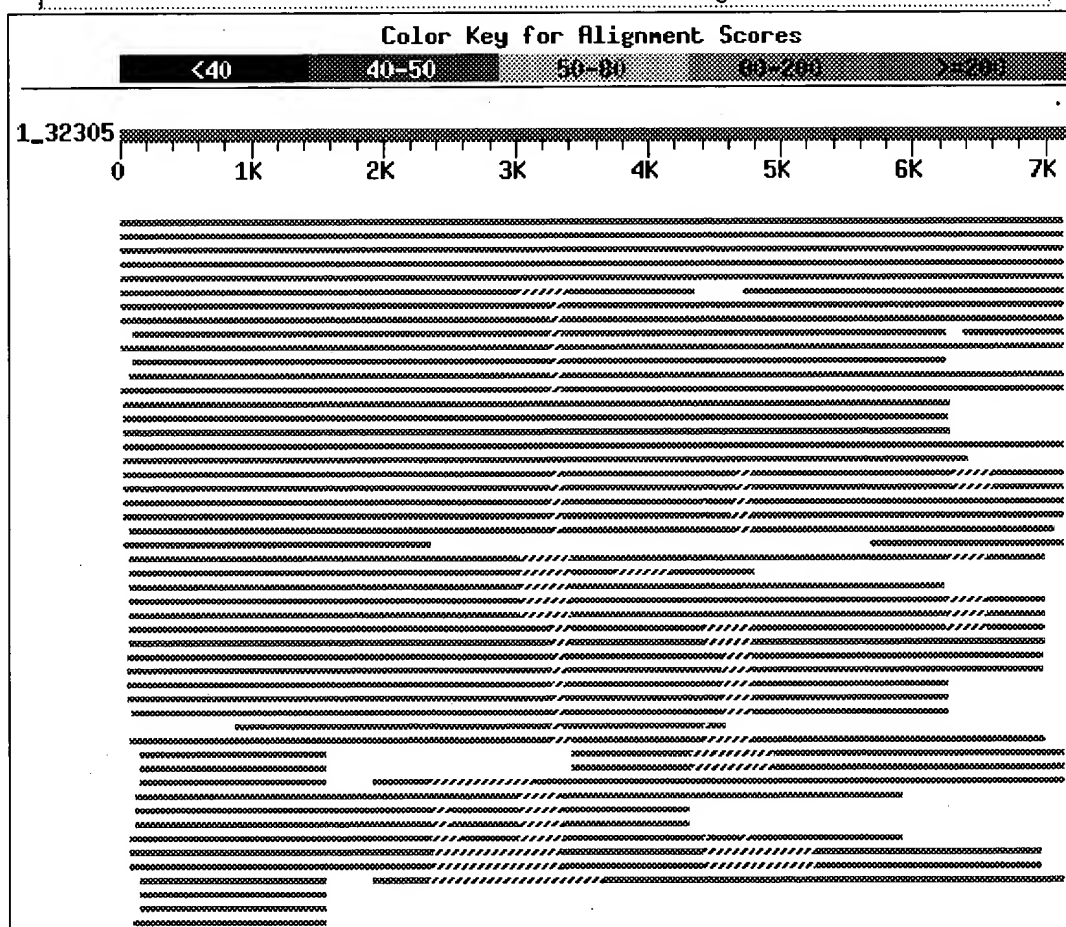
(7211 letters)

Database: All non-redundant GenBank CDS
translations+PDB+SwissProt+PIR+PRF

1,541,362 sequences; 503,870,249 total letters


Taxonomy reports**Distribution of 389 Blast Hits on the Query Sequence**












Mouse-over to show define and scores. Click to show alignments






Sequences producing significant alignments:

Score E
(bits) Value

gi 11066461 gb AAG28596.1 	spectrin-like protein GTRAP41 (R...	1071	0.0	
gi 17367415 sp Q9QWN8 SPCP RAT	Spectrin beta chain, brain 2...	1059	0.0	
gi 38084794 ref XP_129130.3 	spectrin beta 3 [Mus musculus]	1058	0.0	
gi 9507135 ref NP_062040.1 	beta-spectrin 3 [Rattus norvegi...	1057	0.0	
gi 5902122 ref NP_008877.1 	spectrin, beta, non-erythrocyti...	1018	0.0	
gi 30348966 ref NP_787030.1 	spectrin beta 2 isoform 1; bet...	711	0.0	
gi 4507195 ref NP_003119.1 	spectrin, beta, non-erythrocyti...	709	0.0	
gi 30315658 ref NP_842565.1 	spectrin, beta, non-erythrocyt...	699	0.0	
gi 448251 prf 1916380A	beta spectrin (beta fodrin)	698	0.0	
gi 7106421 ref NP_033286.1 	spectrin beta 2 isoform 2; beta...	696	0.0	
gi 34879632 ref XP_240072.2 	similar to Spectrin beta chain...	696	0.0	
gi 18859423 ref NP_571600.1 	spectrin, beta, erythrocytic; ...	577	0.0	
gi 34866100 ref XP_234322.2 	similar to Spectrin beta chain...	553	0.0	
gi 27413156 ref NP_000338.2 	spectrin, beta, erythrocytic (...)	561	0.0	
gi 134798 sp P11277 SPCB HUMAN	Spectrin beta chain, erythro...	560	0.0	
gi 338440 gb AAA60578.1 	spectrin Rouen (beta-220-218) muta...	561	0.0	
gi 7363453 ref NP_038703.1 	spectrin beta 1; beta-spectrin ...	548	0.0	
gi 17647191 ref NP_523388.1 	beta Spectrin CG5870-PA [Droso...	520	0.0	
gi 423777 pir A46147	spectrin beta chain - fruit fly (Dros...	520	0.0	
gi 29179635 gb AAH48851.1 	Similar to beta-spectrin 3 [Mus ...]	721	0.0	
gi 28277312 gb AAH46267.1 	Similar to spectrin, beta, non-e...	741	0.0	
gi 476928 pir A47213	beta-fodrin - human (fragment) >gi 42...	423	0.0	
gi 15213122 gb AAK85734.1 	beta-G spectrin [Brugia malayi]	470	e-177	
gi 17976528 gb AAK77612.2 	Uncoordinated protein 70, isofo...	444	e-161	
gi 5734146 gb AAD49858.1 	beta-G spectrin [Caenorhabditis e...	444	e-161	
gi 17562506 ref NP_504748.1 	beta-G spectrin, UNCoordinated...	444	e-161	
gi 25154697 ref NP_504749.2 	beta-G spectrin, UNCoordinated...	444	e-161	
gi 7505762 pir T29140	hypothetical protein K11C4.3 - Caeno...	442	e-161	
gi 31201697 ref XP_309796.1 	ENSANGP00000012507 [Anopheles ...]	517	e-144	
gi 31201699 ref XP_309797.1 	ENSANGP00000023406 [Anopheles ...]	517	e-144	
gi 226515 prf 1516310A	beta spectrin	461	e-128	
gi 13435161 ref NP_079489.1 	spectrin, beta, non-erythrocyt...	461	e-127	
gi 11602887 gb AAF93171.1 	betaIV spectrin isoform sigma2 [...]	461	e-127	
gi 11602890 gb AAF93173.1 	betaIV spectrin isoform sigma4 [...]	459	e-127	
gi 11992162 gb AAG42473.1 	spectrin beta IV [Homo sapiens]	458	e-127	
gi 17368942 sp Q9H254 SPCQ HUMAN	Spectrin beta chain, brain...	458	e-127	
gi 30794220 ref NP_115999.1 	spectrin beta 4; beta-spectrin...	458	e-127	
gi 16117405 gb AAK38731.1 	beta4-spectrin [Mus musculus] >g...	458	e-127	
gi 338330 gb AAA63259.1 	muscle beta spectrin	259	e-123	
gi 34855389 ref XP_218364.2 	similar to betaIV-spectrin sig...	411	e-112	
gi 2511779 gb AAC79502.1 	beta III spectrin [Homo sapiens]	390	e-106	
gi 444793 prf 1908227A	beta spectrin	320	2e-85	
gi 420115 pir S29854	spectrin beta chain - dog (fragment) ...	316	5e-84	
gi 18481635 gb AAL73492.1 	beta I spectrin form betaI sigma...	245	5e-75	
gi 24656802 ref NP_523900.1 	karst CG12008-PA [Drosophila m...	258	9e-67	
gi 7655 emb CAA37939.1 	betaH spectrin [Drosophila melanoga...	258	9e-67	
gi 103502 pir A37792	spectrin beta-H chain - fruit fly (Dr...	258	1e-66	
gi 31209523 ref XP_313728.1 	ENSANGP00000017034 [Anopheles ...]	250	2e-64	

gi 25155104 ref NP_741632.1 	SMAll body size SMA-1, betaH c...	246	6e-63	
gi 7506776 pir T23630	hypothetical protein R31.1 - Caenorh...	246	6e-63	
gi 13123941 sp Q9QXQ0 AAC4 RAT	Alpha-actinin 4 (Non-muscle ...	213	4e-53	
gi 11230802 ref NP_068695.1 	actinin alpha 4 [Mus musculus]...	213	5e-53	
gi 38197444 gb AAH61788.1 	Actn4 protein [Rattus norvegicus]	213	5e-53	
gi 12025678 ref NP_004915.2 	actinin, alpha 4 [Homo sapiens]...	212	7e-53	
gi 2804273 dbj BAA24447.1 	alpha actinin 4 [Homo sapiens]	212	7e-53	
gi 2493432 sp Q90734 AAC4 CHICK	Alpha-actinin 4 (Non-muscle...	211	2e-52	
gi 32766291 gb AAH54901.1 	Unknown (protein for MGC:63508) ...	207	2e-51	
gi 24639238 ref NP_477484.2 	alpha actinin CG4376-PA [Droso...	204	2e-50	
gi 13928936 ref NP_113863.1 	alpha actinin 4; alpha actinin...	204	2e-50	
gi 17565034 ref NP_506128.1 	actinin (104.1 kD) (atn-1) [Ca...	203	3e-50	
gi 24639240 ref NP_726784.1 	alpha actinin CG4376-PB [Droso...	202	7e-50	
gi 13124689 sp P18091 AACT DROME	Alpha-actinin, sarcomeric ...	202	1e-49	
gi 1070611 pir FAFFAA	alpha-actinin - fruit fly (Drosophil...	201	1e-49	
gi 31242387 ref XP_321624.1 	ENSANGP00000011796 [Anopheles ...	201	2e-49	
gi 2511781 gb AAC79503.1 	beta III spectrin [Homo sapiens]	201	2e-49	
gi 8186 emb CAA36042.1 	unnamed protein product [Drosophila...	200	3e-49	
gi 3157976 gb AAC17470.1 	alpha actinin [Homo sapiens]	199	5e-49	
gi 17137758 ref NP_477485.1 	alpha actinin CG4376-PC [Droso...	198	1e-48	
gi 25992501 gb AAN77132.1 	alpha-actinin [Danio rerio] >gi ...	198	1e-48	
gi 211077 gb AAA48567.1 	actinin [Gallus gallus]	196	7e-48	
gi 13124665 sp P05094 AAC1 CHICK	Alpha-actinin 1 (Alpha-act...	196	7e-48	
gi 539494 pir A42162	alpha-actinin 1 - chicken >gi 211083 ...	196	7e-48	
gi 32766313 gb AAH54911.1 	Unknown (protein for MGC:63559) ...	196	7e-48	
gi 37362178 gb AAQ91217.1 	actinin, alpha 2 [Danio rerio]	195	9e-48	
gi 38018016 gb AAR08137.1 	brain-specific alpha actinin 1 i...	193	3e-47	
gi 13591902 ref NP_112267.1 	actinin, alpha 1; non-muscle a...	193	3e-47	
gi 30585329 gb AAP36937.1 	Homo sapiens actinin, alpha 1 [s...	192	1e-46	
gi 4501891 ref NP_001093.1 	actinin, alpha 1 [Homo sapiens]...	192	1e-46	
gi 32766260 gb AAH54830.1 	Unknown (protein for MGC:62771) ...	192	1e-46	
gi 112959 sp P12814 AAC1 HUMAN	Alpha-actinin 1 (Alpha-actin...	192	1e-46	
gi 63389 emb CAA32079.1 	fibroblast alpha actinin [Gallus g...	192	1e-46	
gi 23394914 gb AAN31639.1 	alpha-actinin [Biomphalaria glab...	191	2e-46	
gi 28193204 emb CAD62344.1 	unnamed protein product [Homo s...	191	2e-46	
gi 34876265 ref XP_214499.2 	similar to actinin, alpha 2 [R...	189	5e-46	
gi 4501893 ref NP_001094.1 	actinin, alpha 2 [Homo sapiens]...	189	5e-46	
gi 31981445 ref NP_150371.2 	actinin alpha 2 [Mus musculus]...	189	6e-46	
gi 32449722 gb AAH43995.2 	Similar to actinin, alpha 1 [Xen...	188	1e-45	
gi 4557241 ref NP_001095.1 	skeletal muscle specific actini...	187	2e-45	
gi 112955 sp P20111 AAC2 CHICK	Alpha-actinin 2 (Alpha actin...	187	2e-45	
gi 19173800 ref NP_596915.1 	actinin alpha 3 [Rattus norveg...	185	9e-45	
gi 7304855 ref NP_038484.1 	actinin alpha 3 [Mus musculus] ...	185	9e-45	
gi 20853961 gb AAM26632.1 	truncated alpha-actinin [Rattus ...	185	9e-45	
gi 13123947 sp Q9JI91 AAC2 MOUSE	Alpha-actinin 2 (Alpha act...	184	2e-44	
gi 555419 gb AAA48566.1 	alpha-actinin	184	3e-44	
gi 7706190 ref NP_057726.1 	spectrin, beta, non-erythrocyti...	182	8e-44	
gi 31242389 ref XP_321625.1 	ENSANGP00000023605 [Anopheles ...	182	1e-43	
gi 2137272 pir I49290	dystonin - mouse (fragment) >gi 9040...	174	3e-41	



gi|19882219|ref|NP_598594.1| dystonin isoform a; bullous pe... 174 3e-41 
 gi|19882221|ref|NP_604443.1| dystonin isoform b; bullous pe... 174 3e-41 
 gi|30315911|sp|Q60824.1 [Segment 1 of 2] Bullous pemphigoi... 173 4e-41 

Alignments

Get selected sequences

Select all

Deselect all

 >gi|11066461|gb|AAG28596.1|  spectrin-like protein GTRAP41 [Rattus norvegicus]
 Length = 2388

Score = 1071 bits (2770), Expect(3) = 0.0

Identities = 750/1295 (57%), Positives = 760/1295 (58%), Gaps = 210/1295 (16%)

Frame = +1

Query: 1 MSSTLSPTDFDSLEIQ-----WDLPSD-----LFERSRIRQYSDINNRRSSS 126
 MSSTLSPTDFDSLEIQ WDLPSD LFERSRI+ +D
 Sbjct: 1 MSSTLSPTDFDSLEIQGQYSDINNRRWDLPSDWDNDSSSARLFERSRIKALAD----- 53

Query: 127 ARDEREAVQKKTFTWDNDKALAKWVNSHLARVTCRVGDLYSXXXXXXXXXXXXXEVLSGET 306
 EREAVQKKTFT KWNNSHLARVTCRVGDLYS EVLSGET
 Sbjct: 54 ---EREAVQKKTFT-----KWNNSHLARVTCRVGDLYSDLRDGRNLLRLLEVLSGET 102

Query: 307 LPKPTKGRMRIHCLENVDKALQFLKE----LENMGSHDIVDGQKVHNHRLTLGLVWTIIL 474
 LPKPTKGRMRIHCLENVDKALQFLKE LENMGSHDIVDG NHRLTLGLVWTIIL
 Sbjct: 103 LPKPTKGRMRIHCLENVDKALQFLKEQKVHLENMGSHDIVDG----NHRLTLGLVWTIIL 158

Query: 475 RF-----EDNKEKK-----CQMKTAGQIQDISVETDALLLWVNVHNFSAKY- 597
 RF EDNKEKK CQMKTAG VNVHNF+ +
 Sbjct: 159 RFQIQDISVETEDNKEKKSADALLLWCQMKTAGYPN-----VNVHNF+TSWR 206

Query: 598 PNLAFNAIVHKHRPDLDDTTSWRDGFESLKKCNAHYNLQNAFNLAKEKLGTLKLLDP--- 768
 LAFNAIVHKHRPDLDD FESLKKCNAHYNLQNAFNLAKEKLGTLKLLDP
 Sbjct: 207 DGLAFNAIVHKHRPDLDD-----FESLKKCNAHYNLQNAFNLAKEKLGTLKLLDPEDV 259

Query: 769 NVDQPDEKSIITYKMKALAVEDVSTYYHYFS-----RIGKVLDHAMEAEASELL 918
 NVDQPDEKSIITY V+TYYHYFS RIGKVLDHAMEAE
 Sbjct: 260 NVDQPDEKSIITY-----VATYYHYFSKMKALAVEGKRIGKVLDHAMEAE----- 304

Query: 919 QWEGKHLVEKYESL-----TIGTFNDRQLANS---VQNQLQSFNSYRTIEQLSGV 1059
 HLVEKYESL TIGTFNDRQLANS VQNQLQSFNSYRT V
 Sbjct: 305 -----HLVEKYESLASELLQWIEQTIGTFNDRQLANSLSGVQNQLQSFNSYRT-----V 353

Query: 1060 EKPPKFTEKGNLEVL---IQSKLRANNQKVY---EGRILFTTPRSDINKAWERLEKAEH 1221
 EKPPKFTEKGNLEVL IQSKLRANNQKVY EGRILI SDINKAWERLEKAEH
 Sbjct: 354 EKPPKFTEKGNLEVLLFTIQSKLRANNQKVYTPREGRLI-----SDINKAWERLEKAEH 407

Query: 1222 ERELALRTEAARFDRENQRLVLIRQEKLEQL-----RETWLS-----FGL 1341
 ERELALRTE LIRQEKLEQL RETWLS FGL
 Sbjct: 408 ERELALRTE-----LIRQEKLEQLAARFDRKAAMRETWLSNQRLVSQDNFGL 455

Query: 1342 ELAKAAMSQDNRKHEAIETDIVAYSGRXXXXXXXXXXXXXXXXXXXXHYHDIKRIAARQN 1521
 EL AA+ RKHEAIETDIVAYSGR HYHDIKRIAARQN
 Sbjct: 456 EL--AAVEAAVRKHEAIETDIVAYSGR-----VQAVDAVAEELAAEHYHDIKRIAARQN 507

Query: 1522 NVARLWDFLREMVAAXXXXXXXXXXXXXQKVFQDLLYLMQSQDLGQLHELVDMWMAEMKGRL- 1698
NVARLWDFLREMVA QKVFQDLLYLM DWMAEMKGRL
Sbjct: 508 NVARLWDFLREMVAARRERLLNLELQKVFQDLLYLM-----DWMAEMKGRLQ 555

Query: 1699 -----KHLAGVEDLLEY-----IAVQAERVRAVSAYRPCGEQSYESALRFCDPGKEXX 1842
KHLAGVEDLL+ IAVQAERVRAVSA SALRFCDPGKE
Sbjct: 556 SQDLGKHLAGVEDLLQLHELVEADIAVQAERVRAVSA-----SALRFCDPGKEYR 605

Query: 1843 ----XXXXXXXXXXPQLVSALCEL-----RRLWRFLWEVGEAEAWVREQQHLLA 1977
Q ALCEL RRLWRFLWEVGEAEAWVREQQHLLA
Sbjct: 606 PCGPQLV SERVATLEQSYEALCELAATRRARLEESRRLWRFLWEVGEAEAWVREQQHLLA 665

Query: 1978 SAETGRDLTGVLRLLNKHTALRGLTLEQGNQASTEMSGRLGPLK-----QQLVAEGHPG 2139
SAETGRDLTGVLRLLNKHTALRG EMSGRLGPLK QQLVAEGHPG
Sbjct: 666 SAETGRDLTGVLRLLNKHTALRG-----EMSGRLGPLKLTLEQGGQQLVAEGHPG 714

Query: 2140 ALQXXXXXXXXXX-----XXXXXXXXXXXXXXXXXSLYQFLVDALRQADANDMEAW----- 2286
A Q SLYQF QADANDMEAW
Sbjct: 715 ANQASTRAAELQAQWERLEALAEERAQRLAQAASLYQF-----QADANDMEAWLVDALR 768

Query: 2287 LVSSPEVGHDEFSTQA-----RALEEEIXXXXXXXXXXXXQHPTLDALREQAA----- 2430
LVSSPEVGHDEFSTQA RALEEEI PTLDALREQAA
Sbjct: 769 LVSSPEVGHDEFSTQALARQHRALEEEI-----RAHRPTLDALREQAAALPPALS 818

Query: 2431 ---EVQGRVPTLEQRARALLSHTPHYEELQARAGE-----FYTMLSEPGACNXXX 2571
EVQGRVPTLEQ HYEELQARAGE FYTMLSE GAC
Sbjct: 819 HTPEVQGRVPTLEQ-----HYEELQARAGERARALEAALAFYTMLSEAGACG--- 865

Query: 2572 XXXXXXXXWVEEKEQWL-----DPEVVQQRFETITAVSPERLELEPEMNALAAR- 2718
WVEEKEQWL DPEVVQQRFET LEPEMNALAAR
Sbjct: 866 -----LWVEEKEQWLNGLALPERLEDPEVVQQRFET-----LEPEMNALAARI 908

Query: 2719 ----DIAEQLLKASPPGKDRIIGTQEQLNQRWQQFRSLAGGKKAALTSALSI----- 2862
DIAEQLLKASPPGKDRIIGTQEQLNQRWQQFRSLAGGKKAALTSALSI
Sbjct: 909 TAVSDIAEQLLKASPPGKDRIIGTQEQLNQRWQQFRSLAGGKKAALTSALSIQNYHLECT 968

Query: 2863 ETQAWMRE-----QDLGNDLAQNYHLECTKTKVIESTGVLALQRKLAGTERDL*ADP 3018
ETQAWMRE QDLGNDLA GVLALQRKLAGTERDL A
Sbjct: 969 ETQAWMREKTKVIESTQDLGNDLA-----GVLALQRKLAGTERDLEA-I 1011

Query: 3019 RAK*SHLCPGGFGCWAPSPSPCHQHTMGGSSGNPGLARRLGEVQ-----TMRRREES 3174
A+ L A P+ P + RLGEVQ TMRRREES
Sbjct: 1012 SARVGELTQEANALAAGHPAQ-----PAINTRLGEVQTGWEDLRATMRRREES 1060

Query: 3175 -----DFLRLSDDFQAWLGRRLQTQTAVASYE 3255
DFLRLSDDFQAWLGR TQTAVAS E
Sbjct: 1061 LGEARRLQDFLRLSDDFQAWLGR---TQTAVASEE 1092

Score = 740 bits (1910), Expect(3) = 0.0

Identities = 536/931 (57%), Positives = 545/931 (58%), Gaps = 144/931 (15%)

Frame = +2

Query: 4775 QAWMGQE-----KAKDELSAQ-----VLEQALALHMMGQEQAQEVKKHDYAQTIKQ 4912
+AWMGQE KAKDELSAQ VLEQALA DYQTIKQ
Sbjct: 1601 EAWMGQELHMMGQEKAKDELSAQAEVKKHQVLEQALA-----DYQTIKQ 1646

Query: 4913 LAASSQDMIDHEHPESTRLTIRGLKELAQAVDKLYA-----RERLQEHLRLCQXX 5065
LAASSQDMIDHEHPESTRLTIR QAVDKLYA RERLQEHLRLCQ

Sbjct: 1647 LAASSQDMIDHEHPESTRITIR-----QAQVDKLYAGLKELAGERRERLQEHRLRCQLR 1700

Query: 5066 XXXXXXXX-----XXXXXSHELGDYEHEQWIERVTMLRDKFREFSRDTDSXXXXXXXXX 5230
SHELGDYEH VTMLRDKFREFSRDT

Sbjct: 1701 RELDDLEQWIEREVVAASHELGDYEH-----VTMLRDKFREFSRDT----- 1743

Query: 5231 XTSTIGQERV-----NGLIAGGH-----EWKDSLNEAWADLLEVALLDTRGQVLAA 5368
STIGQERV NGLIAGGH EWKDSLNEAWADLLE LLDTRGQVLAA

Sbjct: 1744 --STIGQERVDSANALANGLIAGGHAAWATVAEWKDSLNEAWADLLE--LLDTRGQVLAA 1799

Query: 5369 AYELQRFHLHGARQALARVQHKAEEALQRQQQLPDGTGRDLNEHDD-DGRHCAYVQQVQIQ 5545
AYELQRFHLHGARQALARVQHK QQQLPDGTGRDLN + RHCA + IQ

Sbjct: 1800 AYELQRFHLHGARQALARVQHK-----QQQLPDGTGRDLNAAEALQRRHCAY--EHDIQ 1850

Query: 5546 ALSTQ-----LRLQKAYAGDKAQEIQLQTTDGRHMQXXX---XXXXXXXXXXRRQLLL 5692
ALSTQ LRLQKAYAGDKA+EI GRHMQ RRQLLL

Sbjct: 1851 ALSTQVQQVQDDGLRLQKAYAGDKAEEI-----GRHMQAVAEAWAQLQGSSAARRQLLL 1904

Query: 5693 ---DKFRFFKAVREMLLWMAQERPRDKNQQGIKDGINLQM-----DVSSADLVI----- 5830
DKFRFFKAVREMLWM DGINLQM DVSSADLVI

Sbjct: 1905 DTTDKFRFFKAVREMLLWM-----DGINLQMDAQERPRDVSSADLVKNQQ 1950

Query: 5831 ---AEIEARADRFSAACID-----RNHYAAEELQSRMGQELLASEKLSQ----- 5956
AEIEARADRFSAACID RNHYAAEE ISEKLSQ

Sbjct: 1951 GIKAEIEARADRFSAACIDMGQELLARNHYAAEE-----ISEKLSQLQSRRQET 1998

Query: 5957 AEKWQEKMDWXXXXXXXXXXXXXXXXXFGRDAGMAEAWLGCEAF LCSQEPLVRS A-----E 6109
AEKWQEKMDW FGRDAGMAEAW LCSQEPLVRS E

Sbjct: 1999 AEKWQEKMDW---LQLVLEVLVFGRDAGMAEAW-----LCSQEPLVRS AELGCTVDEVE 2049

Query: 6110 SLIKRHTVDEVEQKSAVAWEERFSALEKLTALQERENEQKRKPTSEPRYEE*RRKQP--- 6280
SLIKRH E QKSAVAWEERFSALEKLTAL+ERENEQKRK R EE RRKQP

Sbjct: 2050 SLIKRH---EAFQKSAVAWEERFSALEKLTAL EERENEQKRK-----REEEERRKQPPTS 2101

Query: 6281 -----PEGSLVDGQRVXHTP-QSMASQLDTATQAPSINGVCTDKLPPSTESSQPLLEQQ 6439
PEGSLVDGQRV S+L +TQAPSINGVCTD TESSQPLLEQQ

Sbjct: 2102 EPMASQPEGSLVDGQRVLDTAWDGTQSKLPPSTQAPSINGVCTD-----TESSQPLLEQQ 2156

Query: 6440 RLEQSNVXXXXXXXXXXXXXXXXXXXXDRVERQTLPR-----MPQSRSES SAHVATLPA 6601
RLEQSNV R ERQTLPR MPQSRSES SAHVATLPA

Sbjct: 2157 RLEQSNVP-----EGPGSGTGDESSGPRGERQTLPRGPAPSPMPQSRSES SAHVATLPA 2210

Query: 6602 RGAELSAQE QMEG---RKQEMEAFNKKAYCVLRRGTL CANRSWQNV-----SLGFYKD 6751
RGAELSAQE QMEG RKQEMEAFNKK A ANRSWQNV SLGFYKD

Sbjct: 2211 RGAELSAQE QMEGTL CRKQEMEAFNKK A-----ANRSWQNVYCVLRRGSLGFYKD 2260

Query: 6752 ARAASAGVSLARAQGKRKHVFKLPYHGEVPV-----SVAFDYR-----GLQDGKE 6886
ARAASAGV PYHGEVPV SVAFDYR GLQDGKE

Sbjct: 2261 ARAASAGV-----PYHGEVPVSLARAQGSVAFDYRKRKHVFKLGLQDGKE 2305

Query: 6887 YLFQARVVNAAIAKDEAEMSSWL-----TASSASGXXXXXXXXXXXXGRTRAMTMIV 7042
YLFQ AKDEAEMSSWL TASSASG G TRAMTM

Sbjct: 2306 YLFQ-----AKDEAEMSSWL RVVNAAIATASSASGEPEEPVVP SASRGLTRAMTMPP 2357

Query: 7043 LRKSASRGLSQPEGSEREREREKRFSFFKKNK 7135
+ S L +G EREREKRFSFFKKNK

Sbjct: 2358 VSQPEGSI VLRSKDGREREREKRFSFFKKNK 2388

Score = 496 bits (1278), Expect(3) = 0.0
 Identities = 347/585 (59%), Positives = 356/585 (60%), Gaps = 74/585 (12%)
 Frame = +3

Query: 3258 PSTLPRGETL---GXXXXXXXXXXXXXSRLR-----QADPQCVERAQSEEVTRDR 3401
 P+TLP E L YSRLR QADPQC+ R
 Sbjct: 1094 PATLPEAEALLAQHAALRGEVERAQSEYSRLRTLGEVTRDQADPQCLFL-----R 1144

Query: 3402 QRLEALGTGWHEELGLFLRMWESRQGRLAQAHGFQGFRLRDARQAEGVLTEMPGKLEDFMS 3581
 QRLEALGTGWHEELG RMWESRQGRLAQAHGFQGFRLRDARQAEGVL S
 Sbjct: 1145 QRLEALGTGWHEELG---RMWESRQGRLAQAHGFQGFRLRDARQAEGVL-----S 1189

Query: 3582 SQEYVLSH-----LQAADAAIK-----STMDANGERIRGLLEAGRQLVSKGNIHAEKI 3725
 SQEYVLSH LQAADAAIK STMDANGERIRGLLEAGRQLVSKGNIHAEKI
 Sbjct: 1190 SQEYVLSHTEMPGTLQAADAAIKKLEDFMSSTMDANGERIRGLLEAGRQLVSKGNIHAEKI 1249

Query: 3726 QEKADSIEKRHRKNQEAVQQLLGRRLRDNR----FLQDCQELKLWVSYDEEQQHIDEKMLT 3893
 QEKADSIEKRHRKNQEAVQQLLGRRLRDNR FLQDCQELKLW IDEKMLT
 Sbjct: 1250 QEKADSIEKRHRKNQEAVQQLLGRRLRDNRQHFQDCQELKLW-----IDEKMLT 1300

Query: 3894 AQD-----HTKWQKHQAFMDKVDKARNLAELAANKDWL-----LTLEKPELK 4019
 AQD HTKWQKHQAFM AELAANKDWL LTLEKPELK
 Sbjct: 1301 AQDVSYDEARNLHTKWQKHQAFM-----AELAANKDWLDKVDKEGRELTLEKPELK 1351

Query: 4020 VLRWDELEGREVSEKLEDLHR-----QAKARSLFDANALESWETTTRAELEFAQSCS 4172
 VL VSEKLEDLHR QAKARSLFDAN RAELEFAQSCS
 Sbjct: 1352 VL-----VSEKLEDLHRRWDELETTTQAKARSLFDAN-----RAELEFAQSCS 1393

Query: 4173 -----LESLQAQLHSDDYGKDLTSVNILLKKQQMLEREMAVR*KEVEAIQAQAKALAQED 4337
 LESLQAQLHSDDYGKDLTSVNILLKKQQMLEREMAVR KEVEAIQAQAKALAQED
 Sbjct: 1394 ALESWLESLQAQLHSDDYGKDLTSVNILLKKQQMLEREMAVREKEVEAIQAQAKALAQED 1453

Query: 4338 QSAGE-----SRAVEEKFRALLQ--ASR*KDLSA-HEXXXXXXXXXXXXXDTVGAAPGDRA 4496
 QSAGE SRAVEEKFRAL Q R + L A E P +
 Sbjct: 1454 QSAGEVERTSRAVEEKFRALCQPMKDRCRRLQASREQHQFHRDVEDEILWVTERLPMAS 1513

Query: 4497 ASHGQLSGAWQEEKPDSAPDCRPQRLAQRPAHDGPG*AHSEN-----TEGDRQAELO 4655
 HG+ + Q + Q L + H+P - E G AELO
 Sbjct: 1514 LEHGKDLPSVQLLMK-----KNQTLQKEIQGHEPRIADLKERQRTLRTAAAGPELAELQ 1567

Query: 4656 EMWKRLSHELEAAAAGPELLRGKRLEEALRAQQFYRDAAEARLGWG 4790
 EMWKRLSHELE LRGKRLEEALRAQQFYRDAAEA G
 Sbjct: 1568 EMWKRLSHELE-----LRGKRLEEALRAQQFYRDAAEA EAWMG 1605

Score = 80.5 bits (197), Expect = 4e-13
 Identities = 54/98 (55%), Positives = 56/98 (57%), Gaps = 26/98 (26%)
 Frame = +1

Query: 4411 CQPMKDRCCR-----FHRDVEDEILWEQHQVTERLPMASLEHGK-----KK 4536
 CQPMKDRCCR FHRDVEDEILW VTERLPMASLEHGK KK
 Sbjct: 1474 CQPMKDRCCRRLQASREQHQFHRDVEDEILW----VTERLPMASLEHGKDLPSVQLLMKK 1529

Query: 4537 NQTL-----PRIADLKDLPVQLLMIQGHERTLRT 4626
 NQTL PRIADLK+ +RTLRT
 Sbjct: 1530 NQTLQKEIQGHEPRIADLKE-----RQRTLRT 1556

Score = 37.4 bits (85), Expect = 4.1

Identities = 41/168 (24%), Positives = 72/168 (42%), Gaps = 13/168 (7%)

Frame = +2

Query: 5675 RRQLLLDKFRFFKAVRELMLWMAQERPRDKNQQGIKDGINLQMDVSSADLVIAEIEARAD 5854
R Q ++ +F + V + +LW+ + P + + KD ++Q+ + + EI+

Sbjct: 1483 RLQASREQHQFHRDVEDEILWVTERLPMASSLEHGKDLPSVQLLMKKNQTLQKEIQGHEP 1542

Query: 5855 RFSACIDRNHYAAE-----ELQS--RRMGQELLASEKLSQAEKWQEKMDWXXXXXX 6004
R + +R ELQ +R+ EL ++L +A + Q+

Sbjct: 1543 RIADLKERQRTLRTAAAGPELAELQEMWKRLSHELELRGKRLEEALRAQQ----- 1592

Query: 6005 XXXXXFGRDAGMAEAWLG-CEAFLCSQEPL--VRSAESLIKRTVDE 6139

F RDA AEA+W G E + QE SA++ +K+H V E

Sbjct: 1593 -----FYRDAEAEAWMGQELHMMGQEKAKDELSAQAEVKKHQVLE 1634

Score = 37.0 bits (84), Expect = 5.4

Identities = 70/325 (21%), Positives = 125/325 (38%), Gaps = 15/325 (4%)

Frame = +3

Query: 3405 RLEALGTGWHEELGLFLRMWESRQGRLAQAHGFQGFRLDARQAEGVLTEMPGKLEDFMSS 3584
R L WE L E R RLAQA F DA E L + +

Sbjct: 721 RAAELQAQWERLEALA---EERAQRLAQAASLYQFQADANDMEAWLVDALRLVSSPEVGH 777

Query: 3585 QEYVLSHLQAADAAIKSTMDANGERIRGLLEAGRQLVSKGNIHAEKIQEKADSIEKRHRK 3764
E+ L A++ + A+ + L E L + H ++Q + ++E+ + +

Sbjct: 778 DEFSTQALARQHRALEEEIRAHRTLDALREQAAALPPALS-HTPEVQGRVPTLEQHYEE 836

Query: 3765 NQ----EAVQQLLGRLRDNRLFLQDCQELKLWVSYDEE-----QQHIDEKMLTAQDHT 3908
Q E + L L L + LWV E+ ++ D +++ + T

Sbjct: 837 LQARAGERARALEAALAFYTMSEAGACGLWVEEKEQWLNGLLALPERLEDPEVVQQRFET 896

Query: 3909 KWQKHQAFMDKVDKARNLAELAANKDWLLTLEKPELKVLRWDELEGREVSEKLEDLHRQA 4088
+ A ++ ++AE LL P + + + + ++ L

Sbjct: 897 LEPEMNALAARITAVSDIAEQ-----LLKASPPGKDRIIGTQEQNLNRWQQFRSLAGGK 950

Query: 4089 KARSFLDANALESWE---TTTRAELFAQSCSLESLSQAQLHSDDYGKDLTSVNILLKKQQM 4259
KA +L A +++++ T T+A + ++ +ES Q D G DL V

Sbjct: 951 KA-ALTSALSIQNYHLECTETQAWMREKTKVIESTQ-----DLGNDLAGV-----LA 996

Query: 4260 LEREMAVR*KEVEAIQAQAKALAQE 4334

L+R++A +++EAI A+ L QE

Sbjct: 997 LQRKLAGTERDLEAISARVGELTQE 1021

Score = 36.6 bits (83), Expect = 7.0

Identities = 39/141 (27%), Positives = 58/141 (41%), Gaps = 4/141 (2%)

Frame = +1

Query: 1636 SQDLGQLHELVDWMAEMKGRLLKHLAGVEDLLEYIAVQA----ERVRAVSAYRPCGEQSYE 1803
+QDLG + +A + + LAG E LE I+ + + A++A P +

Sbjct: 984 TQDLG-----NDLAGVLALQRKLAGTERDLEAISARVGELTQEANALAAGHPAQAPAIN 1037

Query: 1804 SALRFCDPGKEXXXXXXXXXXXXXPQLVSALCELRLRLWRFLWEVGEAEAWVREQQHLLASA 1983
+ L G E +L E RRL FL + + +AW+ Q +AS

Sbjct: 1038 TRLGEVQTGWEDLRATMRRE-----ESLGEARRLQDFLRSLDDFQAWLGRGTQTAVASE 1091

Query: 1984 ETGRDLTGVLRLLNKHTALRG 2046
 E L LL +H ALRG
 Sbjct: 1092 EGPATLPEAEALLAQHAALRG 1112

>gi|17367415|sp|Q9QWN8|SPCP_RAT Spectrin beta chain, brain 2 (Spectrin, non-eryt
 (Beta-III spectrin) (SPNB-3) (Beta SpIII sigma 1)
 (Spectrin-like protein GTRAP41)
 gi|3550975|dbj|BAA32699.1| beta-spectrin III [Rattus norvegicus]
 Length = 2388

Score = 1059 bits (2738), Expect(3) = 0.0
 Identities = 746/1295 (57%), Positives = 756/1295 (58%), Gaps = 210/1295 (16%)
 Frame = +1

Query: 1 MSSTLSPTDFDSLEIQ-----WDLPSD-----LFERSRIRQYSDINNRRSS 126
 MSSTLSPTDFDSLEIQ WDLPSD LFERSRI+ +D
 Sbjct: 1 MSSTLSPTDFDSLEIQGQYSDINNRRWDLPSDWDNDSSSARLFERSRIKALAD----- 53

Query: 127 ARDEREAVQKKTFTWDNDKALAKWVNSHLARVTCRVGDLYSXXXXXXXXXXXXEVLSET 306
 EREAVQKKTFT KVVNSHLARVTCRVGDLYS EVLSET
 Sbjct: 54 ---EREAVQKKTFT-----KVVNSHLARVTCRVGDLYSDLRDGRNLLRLLEVLSGET 102

Query: 307 LPKPTKGRMRIHCLENVDKALQFLKE----LENMGSHDIVDGQKVHNHRLTLGLVWTIIL 474
 LPKPTKGRMRIHCLENVDKALQFLKE LENMGSHDIVDG NHRLTLGLVWTIIL
 Sbjct: 103 LPKPTKGRMRIHCLENVDKALQFLKEQKVHLENMGSHDIVDG----NHRLTLGLVWTIIL 158

Query: 475 RF-----EDNKEKK-----CQKMTAGQIQDISVETDALLWVNVHNFSAKY- 597
 RF EDNKEKK CQKMTAG VNVHNF+ +
 Sbjct: 159 RFQIQDISVETEDNKEKKSADALLWCQKMTAGYPN-----VNVHNFTTSWR 206

Query: 598 PNLAFNAIVHKHRPDLLDTSWRDGFESLKKCNAYNLQNAFNLAKEKLGTLKLLDP--- 768
 LAFNAIVHKHRPDLLD FESLKKCNAYNLQNAFNLAKEKLGTLKLLDP
 Sbjct: 207 DGLAFNAIVHKHRPDLLD-----FESLKKCNAYNLQNAFNLAKEKLGTLKLLDPEDV 259

Query: 769 NVDQPDEKSIITYKMKALAVEDVSTYYHYFS-----RIGKVLDHAMEAEASELL 918
 NVDQPDEKSIITY V+TYYHYFS RIGKVLDHAMEAE
 Sbjct: 260 NVDQPDEKSIITY-----VATYYHYFSKMKALAVEGKRIGKVLDHAMEAE----- 304

Query: 919 QWEGKHLVEKYESL-----TIGTFNDRQLANS---VQNQLQSFNSYRTIEQLSGV 1059
 HLVEKYESL TI T NDRQLANS VQNQLQSFNSYRT V
 Sbjct: 305 -----HLVEKYESLASELLQWIEQTIVTLNDRQLANSLSGVQNQLQSFNSYRT-----V 353

Query: 1060 EKPPKFTEKGNLEVL---IQSKLRANNQKVY---EGRLILFTTPRSDINKAWERLEKAEH 1221
 EKPPKFTEKGNLEVL IQSKLRANNQKVY EGRLI SDINKAWERLEKAEH
 Sbjct: 354 EKPPKFTEKGNLEVLLFTIQSKLRANNQKVYTPREGRLI-----SDINKAWERLEKAEH 407

Query: 1222 ERELALRTEAARFDRENQRLVLIRQEKLEQL-----RETWLS-----FGL 1341
 ERELALRTE LIRQEKLEQL RETWLS FGL
 Sbjct: 408 ERELALRTE-----LIRQEKLEQLAARFDRKAAMRETWLSNQRLVSQDNFGL 455

Query: 1342 ELAKAAMSQDNRKHEAIETDIVAYSGRXXXXXXXXXXXXXXXXXXXXHYHDIKRIAARQN 1521
 EL AA+ RKHEAIETDIVAYSGR HYHDIKRIAARQN
 Sbjct: 456 EL--AAVEAAVRKHEAIETDIVAYSGR-----VQAVDAVAEELAAEHYHDIKRIAARQN 507

Query: 1522 NVARLWDFLREMVAAXXXXXXXXXXXXXQKVFQDLLYLMQSQDLGQLHELVDWMAEMKGR- 1698
 NVARLWDFLREMVA QKVFQDLLYLM DWMAEMKGR-
 Sbjct: 508 NVARLWDFLREMVAARRERLLNLELQKVFQDLLYLM-----DWMAEMKGR- 555

Query: 1699 -----KHLAGVEDLLEY-----IAVQAERVRAVSAYRPCGEQSYESALRFCDPGKEXX 1842
KHLAGVEDLL+ IAVQAERVRAVSA SALRFCDPGKE
Sbjct: 556 SQDLGKHLAGVEDLLQLHELVEADIAVQAERVRAVSA-----SALRFCDPGKEYR 605

Query: 1843 -----XXXXXXXXXXPQLVSALCEL-----RRLWRFLWEVGEAEAWVREQQHLLA 1977
Q ALCEL RRLWRFLWEVGEAEAWVREQQHLLA
Sbjct: 606 PCDPQLVSESVATLEQSYEALCELAATRRARLEESRRLWRFLWEVGEAEAWVREQQHLLA 665

Query: 1978 SAETGRDLTGVLRLLNKHTALRGLTLEQGNQASTEMSGRLGPLK-----QQLVAEGHPG 2139
SAETGRDLTGVLRLLNKHTALRG EMSGRLGPLK QQLVAEGHPG
Sbjct: 666 SAETGRDLTGVLRLLNKHTALRG-----EMSGRLGPLKLTLEQGGQLVAEGHPG 714

Query: 2140 ALQXXXXXXXXXX-----XXXXXXXXXXXXXXXXXSLYQFLVDALRQADANDMEAW----- 2286
A Q SLYQF QADANDMEAW
Sbjct: 715 ANQASTRAAELQAQWERLEALAEERAQRLAQAASLYQF-----QADANDMEAWLVDALR 768

Query: 2287 LVSSPEVGHDEFSTQA-----RALEEEIXXXXXXXXXXXQHPTLDALREQAA----- 2430
LVSSPEVGHDEFSTQA RALEEEI PTLDALREQAA
Sbjct: 769 LVSSPEVGHDEFSTQALARQHRALEEEI-----RAHRPTLDALREQAAALPPALS 818

Query: 2431 ---EVQGRVPTLEQRRARALLSHTPHYEELQARAGE-----FYTMLSEPGACNXXX 2571
EVQGRVPTLEQ HYEELQARAGE FYTMLSE GAC
Sbjct: 819 HTPEVQGRVPTLEQ-----HYEELQARAGERARALEAALAFYTMLSEAGACG--- 865

Query: 2572 XXXXXXXXWVEEKEQWL-----DPEVVQQRFETITAVSPERLELEPEMNALAAR- 2718
WVEEKEQWL D EVVQQRFET LEPEMNALAAR
Sbjct: 866 -----LWVEEKEQWLNLGALPERLEDLEVQQRFET-----LEPEMNALAARV 908

Query: 2719 ----DIAEQLLKASPPGKDRIIGTQEQLNQRWQQFRSLAGGKKAALTSALS I----- 2862
DIAEQLLKASPPGKDRIIGTQEQLNQRWQQFRSLA GKKAALTSALS I
Sbjct: 909 TAVSDIAEQLLKASPPGKDRIIGTQEQLNQRWQQFRSLADGKKAALTSALS IQNYHLECT 968

Query: 2863 ETQAWMRE-----QDLGNDLAQNYHLECTKTKVIESTGVLALQRKLAGTERDL*ADP 3018
ETQAWMRE QDLGNDLA GVLALQRKLAGTERDL A
Sbjct: 969 ETQAWMREKTKVIESTQDLGNDLA-----GVLALQRKLAGTERDLEA-I 1011

Query: 3019 RAK*SHLCPPGGFGCWAPSPSPCHQHTMGGSSGNPGLARRLGEVQ-----TMRREES 3174
A+ L A P+ P + RLGEVQ TMRREES
Sbjct: 1012 SARVGELTQEANALAAGHPAQ-----PAINTRLGEVQTGWEDLRATMRREES 1060

Query: 3175 -----DFLRLSDDFQAWLGRRLLQTQTAVASYE 3255
DFLRLSDDFQAWLGR TQTAVAS E
Sbjct: 1061 LGEARRLQDFLRLSDDFQAWLGR---TQTAVASEE 1092

Score = 740 bits (1910), Expect(3) = 0.0
Identities = 536/931 (57%), Positives = 545/931 (58%), Gaps = 144/931 (15%)
Frame = +2

Query: 4775 QAWMGQE-----KAKDELSAQ-----VLEQALALHMMGQEQAQVKKHDYAQTIKQ 4912
+AWMGQE KAKDELSAQ VLEQALA DYQTIKQ
Sbjct: 1601 EAWMGQELHMMGQEKAKDELSAQAEVKKHQVLEQALA-----DYQTIKQ 1646

Query: 4913 LAASSQDMIDHEHPESTRLTIRGLKELAQAVDKLYA-----RERLQEHLRLCQXX 5065
LAASSQDMIDHEHPESTRLTIR QAQVDKLYA RERLQEHLRLCQ
Sbjct: 1647 LAASSQDMIDHEHPESTRLTIR-----QAQVDKLYAGLKLAGEERRERLQEHLRLCQLR 1700

Query: 5066 XXXXXXXX-----XXXXXSHELGDYEHEQWIQERVMTLRDKFREFSRDTDSXXXXXXXXX 5230



results of BLAST

BLASTN 2.2.6 [Apr-09-2003]

Query:

Database: nr

Fields: Query id, Subject id, % identity, alignment length, mismatches, gap openin

1_30527	gi 3452552 dbj AB001347.1	92.00	300	0	12	193	480
1_30527	gi 3452552 dbj AB001347.1	81.75	515	42	45	3633	4115
1_30527	gi 3452552 dbj AB001347.1	86.09	381	9	22	4173	4530
1_30527	gi 3452552 dbj AB001347.1	84.07	427	9	24	4142	4530
1_30527	gi 3452552 dbj AB001347.1	98.96	193	2	0	1440	1632
1_30527	gi 3452552 dbj AB001347.1	100.00	144	0	0	1903	2046
1_30527	gi 3452552 dbj AB001347.1	98.65	148	2	0	2719	2866
1_30527	gi 3452552 dbj AB001347.1	95.92	147	0	2	5285	5431
1_30527	gi 3452552 dbj AB001347.1	100.00	121	0	0	7091	7211
1_30527	gi 3452552 dbj AB001347.1	93.75	144	0	2	673	807
1_30527	gi 3452552 dbj AB001347.1	86.87	198	7	11	2686	2866
1_30527	gi 3452552 dbj AB001347.1	91.84	147	1	4	3398	3543
1_30527	gi 3452552 dbj AB001347.1	93.33	135	0	6	6551	6676
1_30527	gi 3452552 dbj AB001347.1	100.00	91	0	0	4888	4978
1_30527	gi 3452552 dbj AB001347.1	98.89	90	1	0	6146	6235
1_30527	gi 3452552 dbj AB001347.1	98.90	91	0	1	4709	4798
1_30527	gi 3452552 dbj AB001347.1	86.76	136	0	7	5624	5741
1_30527	gi 3452552 dbj AB001347.1	81.54	195	8	19	5561	5741
1_30527	gi 3452552 dbj AB001347.1	98.70	77	0	1	1176	1252
1_30527	gi 3452552 dbj AB001347.1	91.09	101	0	4	5957	6057
1_30527	gi 3452552 dbj AB001347.1	84.06	138	12	10	6865	6997
1_30527	gi 3452552 dbj AB001347.1	90.62	96	0	1	1057	1143
1_30527	gi 3452552 dbj AB001347.1	84.25	127	5	9	5024	5135
1_30527	gi 3452552 dbj AB001347.1	87.50	96	0	4	2143	2238
1_30527	gi 3452552 dbj AB001347.1	98.18	55	1	0	6406	6460
1_30527	gi 3452552 dbj AB001347.1	88.10	84	4	5	4610	4688
1_30527	gi 3452552 dbj AB001347.1	91.55	71	3	3	2937	3006
1_30527	gi 3452552 dbj AB001347.1	82.35	119	10	10	6281	6392
1_30527	gi 3452552 dbj AB001347.1	83.19	113	6	9	5453	5560
1_30527	gi 3452552 dbj AB001347.1	100.00	49	0	0	1375	1423
1_30527	gi 3452552 dbj AB001347.1	87.36	87	2	2	961	1038
1_30527	gi 3452552 dbj AB001347.1	100.00	48	0	0	604	651
1_30527	gi 3452552 dbj AB001347.1	100.00	48	0	0	1	48
1_30527	gi 3452552 dbj AB001347.1	100.00	47	0	0	3050	3096
1_30527	gi 3452552 dbj AB001347.1	100.00	45	0	0	6731	6775
1_30527	gi 3452552 dbj AB001347.1	100.00	45	0	0	5831	5875
1_30527	gi 3452552 dbj AB001347.1	100.00	45	0	0	5156	5200
1_30527	gi 3452552 dbj AB001347.1	84.38	96	0	8	2287	2367
1_30527	gi 3452552 dbj AB001347.1	100.00	42	0	0	1733	1774
1_30527	gi 3452552 dbj AB001347.1	100.00	39	0	0	865	903
1_30527	gi 3452552 dbj AB001347.1	100.00	36	0	0	6074	6109
1_30527	gi 3452552 dbj AB001347.1	100.00	36	0	0	3291	3326
1_30527	gi 3452552 dbj AB001347.1	100.00	36	0	0	133	168
1_30527	gi 3452552 dbj AB001347.1	100.00	34	0	0	6923	6956
1_30527	gi 3452552 dbj AB001347.1	100.00	34	0	0	2431	2464
1_30527	gi 3452552 dbj AB001347.1	100.00	34	0	0	2398	2431
1_30527	gi 3452552 dbj AB001347.1	100.00	33	0	0	2590	2622
1_30527	gi 3452552 dbj AB001347.1	100.00	33	0	0	2494	2526
1_30527	gi 3452552 dbj AB001347.1	97.22	36	1	0	2256	2291
1_30527	gi 3452552 dbj AB001347.1	100.00	33	0	0	2110	2142
1_30527	gi 3452552 dbj AB001347.1	100.00	32	0	0	1667	1698
1_30527	gi 3452552 dbj AB001347.1	97.06	34	1	0	4793	4826

1_30527	gi 3452552 dbj AB001347.1	100.00	31	0	0	2080	2110
1_30527	gi 3452552 dbj AB001347.1	100.00	30	0	0	6494	6523
1_30527	gi 3452552 dbj AB001347.1	100.00	30	0	0	3873	3902
1_30527	gi 3452552 dbj AB001347.1	100.00	30	0	0	1699	1728
1_30527	gi 3452552 dbj AB001347.1	100.00	30	0	0	1285	1314
1_30527	gi 3452552 dbj AB001347.1	96.88	32	1	0	5229	5260
1_30527	gi 3452552 dbj AB001347.1	100.00	29	0	0	523	551
1_30527	gi 3452552 dbj AB001347.1	100.00	28	0	0	3606	3633
1_30527	gi 3550974 dbj AB008551.1	92.00	300	0	12	193	480
1_30527	gi 3550974 dbj AB008551.1	81.78	516	40	43	3633	4115
1_30527	gi 3550974 dbj AB008551.1	86.09	381	9	24	4173	4530
1_30527	gi 3550974 dbj AB008551.1	84.07	427	9	24	4142	4530
1_30527	gi 3550974 dbj AB008551.1	99.48	193	1	0	1440	1632
1_30527	gi 3550974 dbj AB008551.1	100.00	144	0	0	1903	2046
1_30527	gi 3550974 dbj AB008551.1	98.65	148	2	0	2719	2866
1_30527	gi 3550974 dbj AB008551.1	95.92	147	0	2	5285	5431
1_30527	gi 3550974 dbj AB008551.1	100.00	121	0	0	7091	7211
1_30527	gi 3550974 dbj AB008551.1	93.75	144	0	2	673	807
1_30527	gi 3550974 dbj AB008551.1	93.15	146	1	1	3398	3543
1_30527	gi 3550974 dbj AB008551.1	86.87	198	7	11	2686	2866
1_30527	gi 3550974 dbj AB008551.1	93.33	135	0	6	6551	6676
1_30527	gi 3550974 dbj AB008551.1	100.00	91	0	0	4888	4978
1_30527	gi 3550974 dbj AB008551.1	98.89	90	1	0	6146	6235
1_30527	gi 3550974 dbj AB008551.1	98.90	91	0	1	4709	4798
1_30527	gi 3550974 dbj AB008551.1	86.76	136	0	7	5624	5741
1_30527	gi 3550974 dbj AB008551.1	81.54	195	8	19	5561	5741
1_30527	gi 3550974 dbj AB008551.1	98.70	77	0	1	1176	1252
1_30527	gi 3550974 dbj AB008551.1	91.09	101	0	4	5957	6057
1_30527	gi 3550974 dbj AB008551.1	84.06	138	12	10	6865	6997
1_30527	gi 3550974 dbj AB008551.1	90.62	96	0	1	1057	1143
1_30527	gi 3550974 dbj AB008551.1	84.25	127	5	9	5024	5135
1_30527	gi 3550974 dbj AB008551.1	87.50	96	0	4	2143	2238
1_30527	gi 3550974 dbj AB008551.1	98.18	55	1	0	6406	6460
1_30527	gi 3550974 dbj AB008551.1	88.10	84	4	5	4610	4688
1_30527	gi 3550974 dbj AB008551.1	91.55	71	3	3	2937	3006
1_30527	gi 3550974 dbj AB008551.1	82.35	119	10	10	6281	6392
1_30527	gi 3550974 dbj AB008551.1	83.19	113	6	9	5453	5560
1_30527	gi 3550974 dbj AB008551.1	100.00	49	0	0	1375	1423
1_30527	gi 3550974 dbj AB008551.1	87.36	87	2	2	961	1038
1_30527	gi 3550974 dbj AB008551.1	100.00	48	0	0	604	651
1_30527	gi 3550974 dbj AB008551.1	100.00	48	0	0	1	48
1_30527	gi 3550974 dbj AB008551.1	100.00	47	0	0	3050	3096
1_30527	gi 3550974 dbj AB008551.1	100.00	45	0	0	6731	6775
1_30527	gi 3550974 dbj AB008551.1	100.00	45	0	0	5831	5875
1_30527	gi 3550974 dbj AB008551.1	100.00	45	0	0	5156	5200
1_30527	gi 3550974 dbj AB008551.1	84.38	96	0	8	2287	2367
1_30527	gi 3550974 dbj AB008551.1	100.00	42	0	0	1733	1774
1_30527	gi 3550974 dbj AB008551.1	100.00	39	0	0	865	903
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1_30527	gi 3550974 dbj AB008551.1	100.00	36	0	0	3291	3326
1_30527	gi 3550974 dbj AB008551.1	100.00	36	0	0	133	168
1_30527	gi 3550974 dbj AB008551.1	100.00	34	0	0	6923	6956
1_30527	gi 3550974 dbj AB008551.1	100.00	34	0	0	2431	2464
1_30527	gi 3550974 dbj AB008551.1	100.00	34	0	0	2398	2431
1_30527	gi 3550974 dbj AB008551.1	100.00	33	0	0	2590	2622
1_30527	gi 3550974 dbj AB008551.1	100.00	33	0	0	2494	2526
1_30527	gi 3550974 dbj AB008551.1	97.22	36	1	0	2256	2291
1_30527	gi 3550974 dbj AB008551.1	100.00	33	0	0	2110	2142
1_30527	gi 3550974 dbj AB008551.1	100.00	32	0	0	3961	3992
1_30527	gi 3550974 dbj AB008551.1	100.00	32	0	0	1667	1698

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=> S SPECTRIN AND RATTUS
L2 2 SPECTRIN AND RATTUS

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PROCESSING COMPLETED FOR L2
L3 2 DUP REM L2 (0 DUPLICATES REMOVED)

=> D 1

L3 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:161955 BIOSIS
DN PREV200200161955
TI Synaptic scaffolding proteins in rat brain. Ankyrin repeats of the
multidomain Shank protein family interact with the cytoskeletal protein
alpha-fodrin.
AU Boeckers, Tobias M.; Mameza, Marie Germaine; Kreutz, Michael R.; Bockmann,
Juergen; Weise, Christoph; Buck, Fritz; Richter, Dietmar [Reprint author];
Gundelfinger, Eckart D. [Reprint author]; Kreienkamp, Hans-Juergen
CS Institut fuer Zellbiochemie und klinische Neurobiologie, Universitaet
Hamburg, Martinistrasse 52, 20246, Hamburg, Germany
richter@uke.uni-hamburg.de; gundelfinger@ifn-magdeburg.de
SO Journal of Biological Chemistry, (October 26, 2001) Vol. 276, No. 43, pp.
40104-40112. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 21 Feb 2002
Last Updated on STN: 26 Feb 2002

=> D 2

L3 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1998:472526 BIOSIS
DN PREV199800472526
TI Ancient large-scale genome duplications: Phylogenetic and linkage analyses
shed light on chordate genome evolution.
AU Pebusque, Marie-Josephe; Coulier, Francois; Birnbaum, Daniel [Reprint
author]; Pontarotti, Pierre

CS Inst Cancerologie d'Immunologie de Marseille, Univ. Mediterranee, INSERM U
119, 27 Bd Lei Roure 13009 Marseille, France
SO Molecular Biology and Evolution, (Sept., 1998) Vol. 15, No. 9, pp.
1145-1159. print.
CODEN: MBEVEO. ISSN: 0737-4038.
DT Article
LA English
ED Entered STN: 5 Nov 1998
Last Updated on STN: 5 Nov 1998

=> S GTRAP41 AND RATTUS
L4 0 GTRAP41 AND RATTUS

=> S GTRAP* AND RATTUS
L5 0 GTRAP* AND RATTUS

=> S SPNB3 AND RATTUS
L6 0 SPNB3 AND RATTUS

=> S SPN* AND RATTUS
L7 0 SPN* AND RATTUS

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FULL ESTIMATED COST

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ENTRY	SESSION
6.22	6.49

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